

(1390 REV. 5-93) US DEPT. OF COMMERCE PATENT & TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER
111504

**TRANSMITTAL LETTER TO THE
UNITED STATES
DESIGNATED/ELECTED OFFICE
(DO/EO/US) CONCERNING A FILING
UNDER 35 U.S.C. 371**

U.S. APPLICATION NO.
(if known, sec 37 C.F.R.1.5)

10/018469

INTERNATIONAL APPLICATION NO.
PCT/FR00/01848INTERNATIONAL FILING DATE
June 30, 2000PRIORITY DATE CLAIMED
July 16, 1999

TITLE OF INVENTION
NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A SHOCK WAVE THROUGH A WALL

APPLICANTS FOR DO/EO/US
Patrick ALEXANDRE, Pierre BRUNET, Brigitte CAGNON, Claude MIKLER

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☒ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.
☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. ☐ A substitute specification.
15. ☐ Entitlement to small entity status is hereby asserted.
16. ☐ Other items or information:

U.S. APPLICATION NO. (known) see 37
C.F.R. 1.5) 10/018469INTERNATIONAL APPLICATION NO.
PCT/FR00/01848ATTORNEY'S DOCKET NUMBER
111504

- 17.
- ☒
- The following fees are submitted:

Basic National fee (37 CFR 1.492(a)(1)-(5)):

Search Report has been prepared by the EPO or JPO\$890.00

International preliminary examination fee paid to USPTO
(37 CFR 1.482)\$710.00No international preliminary examination fee paid to USPTO
(37 CFR 1.482) but international search fee paid to USPTO
(37 CFR 1.445(a)(2))\$740.00Neither international preliminary examination fee (37 CFR
1.482) nor international search fee (37 CFR 1.445(a)(2))
paid to USPTO\$1,040.00International preliminary examination fee paid to USPTO
(37 CFR 1.482) and all claims satisfied provisions of PCT
Article 33(2)-(4)\$ 100.00**ENTER APPROPRIATE BASIC FEE AMOUNT =**

\$890.00

Surcharge of \$130.00 for furnishing the oath or declaration later than
☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR
1.492(e)).

\$

Claims	Number Filed	Number Extra	Rate	
Total Claims	10- 20 =	0	X \$ 18.00	\$
Independent Claims	1- 3 =	0	X \$ 84.00	\$
Multiple dependent claim(s) (if applicable)			+ \$280.00	\$

TOTAL OF ABOVE CALCULATIONS =

\$890.00

Reduction by 1/2 for filing by small entity, if applicable.

- \$

SUBTOTAL =

\$890.00

Processing fee of \$130.00 for furnishing the English translation later
than ☐ 20 ☐ 30 month from the earliest claimed priority date (37 CFR
1.492(f)).

\$

TOTAL NATIONAL FEE =

\$890.00

Amount to be
refunded \$

Charged \$

- a. ☒ Check No. 126130 in the amount of \$890.00 to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. _____ in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 15-0461. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320Date: December 19, 2001NAME: William P. Berridge
REGISTRATION NUMBER: 30,024NAME: Joel S. Armstrong
REGISTRATION NUMBER: 36,430

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Patrick ALEXANDRE, Pierre BRUNET,
Brigitte CAGNON, Claude MIKLERApplication No.: U.S. National Stage
of PCT/FR00/01848

Filed: December 19, 2001

Docket No.: 111504

For: NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A SHOCK
WAVE THROUGH A WALLPRELIMINARY AMENDMENTDirector of the U.S. Patent and Trademark Office
Washington, D. C. 20231

Sir:

Prior to initial examination, and after entry of the annexes to the IPER, please amend
the above-identified application as follows:

IN THE CLAIMS:

Please replace claims 3, and 5-9 as follows:

3. (Amended) The needleless syringe as claimed in claim 1, characterized in that the shock wave generator device (3) produces a plane shock wave on the upstream face (5) of the fixed barrier (4).
5. (Amended) The needleless syringe as claimed in claim 1, characterized in that each cavity (7) has a form of revolution about an axis parallel to the direction of propagation of the shock wave.
6. (Amended) The needleless syringe as claimed in claim 1, characterized in that a plurality of cavities are distributed on the downstream face (6) of said barrier (4).

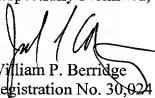
7. (Amended) The needleless syringe as claimed in claim 1, characterized in that the shock wave on the upstream face (5) of the fixed barrier (4) is produced by a weight which impacts said barrier (4).
8. (Amended) The needleless syringe as claimed in claim 1, characterized in that the device (3) generating a shock wave on the upstream face (5) of the fixed barrier (4) comprises a detonating pyrotechnic charge.
9. (Amended) The needleless syringe as claimed in claim 1, characterized in that the length of the application guide (8) is between 1 and 8 times the diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

REMARKS

Claims 1-10 are pending. By this Preliminary Amendment, claims 3 and 5-9 are amended to eliminate multiple dependencies. Prompt and favorable examination on the merits is respectfully requested.

The attached Appendix includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

Respectfully submitted,


William P. Berridge
Registration No. 30,924

Joel S. Armstrong
Registration No. 36,430

JAO:JSA/cmm

Attachment: Appendix

Date: December 19, 2001

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461
--

APPENDIX

Changes to Claims:

The following are marked-up versions of the amended claims:

3. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 2,~~
characterized in that the shock wave generator device (3) produces a plane shock wave on the
upstream face (5) of the fixed barrier (4).
5. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 4,~~
characterized in that each cavity (7) has a form of revolution about an axis parallel to the
direction of propagation of the shock wave.
6. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 4,~~
characterized in that a plurality of cavities are distributed on the downstream face (6) of said
barrier (4).
7. (Amended) The needleless syringe as claimed in claim 1 ~~one of claims 1 to 3,~~
characterized in that the shock wave on the upstream face (5) of the fixed barrier (4) is
produced by a weight which impacts said barrier (4).
8. (Amended) The needleless syringe as claimed in claim 1 ~~one of claims 1 to 3,~~
characterized in that the device (3) generating a shock wave on the upstream face (5) of the
fixed barrier (4) comprises a detonating pyrotechnic charge.
9. (Amended) The needleless syringe as claimed in claim 1 ~~one of the preceding claims,~~
characterized in that the length of the application guide (8) is between 1 and 8 times the
diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

i/PRTS

10/018469

531 Rec'd PCT/ 19 DEC 2001

PCT/FR00/01848

WO 01/05451

NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A
SHOCK WAVE THROUGH A WALL.

The present invention is in the field of needleless
5 syringes used for intradermal, subcutaneous or,
intramuscular injections of various active principles
for therapeutic use in human or veterinary medicine.

Many types of needleless syringes for injecting liquid
10 active principles have been known since 1945. In these
devices, the liquid active principle is delivered, via
a nozzle comprising at least one orifice, by a piston
or by the deformation of a flexible envelope containing
said liquid, said flexible envelope being connected to
15 the nozzle. The injection pressure is obtained either
by the release of an initially compressed spring or by
the release of a gas stored under pressure, as is
described in US Patent 3,788,315. Other subcutaneous
injection devices use a pyrotechnic charge generating
20 gas to propel a piston which delivers the liquid to be
injected, and US Patent 3,802,430 illustrates such a
technique for generating propellant gas.

For injecting solid active principles in the form of a
25 dry powder, needleless syringes use different means to
accelerate the particles of said active principle, and
mention must be made of patent application WO 94/24263

which describes a needleless syringe in which the particles of the active principle are entrained by a gas flow at high speed, by means of a compressed gas being released through a tubing. Despite the use of a long tubing, a dispersed cloud of particles is produced, which suggests that there is a low bioavailability. Auxiliary devices also have to be used to dissipate the blast effect and noise of the gas jet. Finally, the reliability of the system depends on that of the device used for storing the gases under pressure.

In another technical field, US Patent 4,945,050 describes the principle of a laboratory apparatus for bombarding a cell culture with metal microparticles coated with various biological substances for purposes of gene transfection. Different means are used in particular to transfer the kinetic energy of a projectile impacting a barrier to the particles arranged on the projectile or on this barrier and to cause these particles to penetrate into the cell culture. This laboratory apparatus operates under a vacuum and uses very dense neutral microparticles to increase the kinetic energy (microparticles of gold or of tungsten), which excludes any application or any transposition as a needleless syringe, especially since it produces a cloud of particles in order to reach the largest possible number of cells.

One of the objects of the invention is to overcome the disadvantages affecting needleless syringes permitting injection of powdered active principle. Another object
5 of the present invention is to make available a more universal syringe which can be used for injection not only of powdered active principles but also of active principles which are liquid, or in suspension in a liquid, or in the form of gel. The transformation of
10 the initial volume of the active principle and its streamlining at the moment of penetration into the skin are obtained by an effect of reversal and focusing which has been discovered and which has been observed in the case of liquids, gels and powders.

15 The present invention relates to a needleless syringe for injecting active principle for therapeutic use, comprising, from upstream to downstream, a propelling system, the active principle, and an application guide
20 for applying said syringe to the skin of the subject to be treated, this syringe being such that, on the one hand, the propelling system consists of a shock wave generator device and, on the other hand, the active principle is arranged in at least one blind cavity of
25 the downstream face of a barrier continued by the application guide. The barrier in fact has two opposite faces, namely an upstream one, situated toward the shock wave generator device, and another, the

downstream one, situated toward the application guide.

The upstream face of the barrier is substantially plane and transverse. The downstream face of the fixed barrier comprises at least one blind cavity, this cavity thus having an opening only on the downstream face of the fixed barrier and not opening out on the upstream face, thereby providing a thickness sufficient to resist the shock wave.

The shock wave generator device advantageously produces a plane shock wave on the upstream face of the fixed barrier. The plane shock wave produced on the upstream face of the fixed barrier propagates through this barrier and violently ejects the active principle from each of the cavities where it was arranged. Unexpectedly, the active principle thus accelerated at very high speed is able to regroup in the form of a central jet of small diameter which will then penetrate into the skin of the subject. Each jet corresponds to a cavity and has a streamlined shape at its downstream end once the distance traveled by this jet corresponds to several diameters from the fixed barrier. It should be noted that the phenomenon of ejection in the form of jets is fully effective when the shock wave is plane at the moment when it reaches the cavities. This does not exclude the possibility that the shock wave produced on the upstream face may not be strictly plane and may

have a slight curvature, which will be eliminated upon propagation in the barrier.

This phenomenon of shaping into a streamlined jet of
5 active principle starting from the principle initially
stored in globular form, in all or part of a cavity
subjected to a shock wave, can be likened to the jets
of substance which result from the detonation of
explosive charges having a concave downstream face
10 covered by a metal foil. Such explosive charges,
referred to as "hollow charges", make it possible to
obtain streamlined shards at high temperature which are
propelled at speeds of the order of 8000 meters per
second and are capable of piercing armored plating of
15 up to 1 meter in thickness. However, the phenomenon
employed in the present invention is of an entirely
different nature since the active principle must not in
practice experience any increase in temperature and
propulsion speeds of the order of 600 to 1000 meters
20 per second are entirely sufficient to permit an
injection through the epidermis. In contrast to the
explosive charges forming a central jet of substance,
the explosive must not be in contact with the
substance to be ejected and must be separated by a
25 resistant barrier which ensures a good propagation of
the shock wave, which barrier can be made, for example,
of aluminum or steel. On account of the limited speed
of ejection of the jet of active principle, it was

discovered that not only could the shock wave be obtained with a small quantity of explosive whose detonation is triggered by a microdetonator, but that this shock wave could be obtained by other means such as the propulsion of a weight which strikes the upstream face of the fixed barrier.

Advantageously, to obtain a streamlined jet, each blind cavity of the fixed barrier has an opening transverse section which is at least equal to each transverse section of this cavity and preferably each cavity has a form of revolution about an axis parallel to the direction of propagation of the shock wave, with the aim of promoting the formation of a jet which is perfectly aligned on the axis of said cavity.

A cavity can preferably have, for example, a hemispherical, conical or frustoconical shape or can consist of a combination of these profiles.

According to an alternative embodiment, a plurality of cavities are distributed on the downstream face of the barrier. These cavities, which can have different shapes, are advantageously distributed uniformly on said surface.

The active principle is advantageously deposited at the bottom of the cavity and preferably fills the whole

cavity until it is flush with the plane part of the downstream face in which it is retained, for example, by means of a thin film. This is because digital simulations have shown that with such a configuration of filling, the diametrical dispersion of the jet is minimal.

The material used for the fixed barrier is chosen from the group of materials which do not give rise to the phenomenon of flaking under the action of a shock wave, such as, for example, metals. It is also chosen on the basis of its density and its acoustic impedance, in other words its ability to transmit the shock wave. It is in particular chosen as a function of the speed one wishes to communicate to the jet.

In a first embodiment, the shock wave on the upstream face of the fixed barrier is produced by the impact, on said upstream face, of a weight of suitable shape which is accelerated by an auxiliary device. The diameter of said weight is advantageously such that the air located between the weight and the fixed barrier is expelled without braking said weight, which is guided by suitable means. The acceleration of the weight is effected either by the release of a compressed spring or by the combustion of a pyrotechnic charge, or by the release of compressed gas.

In a second embodiment, the plane shock wave on the upstream face of the fixed barrier is produced by a shock wave generator which comprises a detonating pyrotechnic charge. The latter advantageously comprises a foil of explosive adjacent to the upstream face, said foil of explosive being triggered either at a point or over all or part of its surface by a microdetonator. This foil of explosive has a diameter substantially equal to that of the fixed barrier and comprises several tens of milligrams of an explosive such as TNT or a composite explosive with a high speed of detonation.

- 15 The application guide has a length which is such that it allows the active principle, during its ejection toward the skin, to regroup in the form of a streamlined jet. The length of the application guide is advantageously between 1 and 8 times the diameter of the fixed barrier and preferably between 2 and 5 times the diameter of the fixed barrier.

The application guide advantageously comprises a shock absorbing system which can be reduced to a simple flexible flange situated at its end bearing on the skin of the subject to be treated, or can consist of a telescopic application guide with an inner spring.

The present invention satisfactorily solves the problems posed and makes it possible, for example, to obtain, for a barrier of 5 mm diameter and 2 mm thickness, jets of diameters between 0.12 mm and 1.6 mm when use is made of ogival, substantially hemispherical or conical cavities, although in the case of conical cavities in particular it is advantageous if the downstream face of the active principle is plane and does not exceed 3 to 4 mm in diameter.

For a barrier with a diameter of 5 millimeters, a thickness of 3 millimeters and a hemispherical cavity of one millimeter radius, using an explosive pellet with a diameter of 3 millimeters and a thickness of 1 millimeter, it is possible to obtain a jet having a maximum diameter of 0.7 millimeter with a speed of ejection of 630 meters per second.

The major effect sought using the ejection device according to the invention is an attenuated effect referred to as "hollow charge" which translates into the formation of a streamlined jet composed of the particles of substance to be expelled, and driven, on its axis, at a very high speed which gives it a high force of penetration. The characteristics of this jet, namely its shape, its length, its dispersion and its speed of displacement are a function of the nature and

positioning of the generator of plane waves, the material constituting the part serving as barrier, and the geometry of the cavities in the downstream face serving to accommodate the particles. At a lower level, 5 the general shape of the volume formed by the particles in each cavity also plays a role.

Advantageously, under the effect of the pyrotechnic charge, the barrier, although having been deformed, 10 remains fixed in the syringe at its original position. According to another embodiment of the invention, when confronted by the same stress the barrier is displaced but remains trapped in the syringe without any possibility of being expelled.

15 The application guide is preferably made up of a hollow cylindrical body whose cross section is similar to that formed by the downstream face of the barrier and whose axis is perpendicular to said face. This guide is 20 particularly recommended for optimizing the conditions for achieving a perpendicular impact on said surface.

According to a first embodiment of the invention, the particles form a mass of powder in each cavity. These 25 particles are held in their seat by capillarity, by static electricity, by an adhesive surface state or by a membrane covering each cavity. Finally, any means of adhesion can be used, provided that it does not

interfere with the formation of the jet.

According to a second embodiment of the invention, the particles are bound to each other by a liquid which is
5 fluid, viscous or in the form of a gel. In relation to this liquid, the particles of active principle can be either in suspension or in solution.

Advantageously, the trigger can be a push button which
10 initiates the microdetonator by percussion.

The device according to the invention has the advantage of being efficient while having a simple and lightweight design which takes up little space. This is
15 because the technique involving the formation of a jet using the hollow charge model allows particles to be projected in concentrated form and at very high speed from a device having a small number of components made of lightweight materials and arranged in a simple
20 manner in relation to one another.

Moreover, a rapid dimensioning makes it possible to adapt the device to a wide range of situations, by acting in particular on the cross section of the jet,
25 its dispersion, its length, its speed, and the number of jets to be expelled.

Furthermore, as the active principle is not set in motion by the release of the gases, there is no hissing effect. Nor is there any noise associated with the release of the gases to the outside, the noise only
5 possibly originating from the impact of the weight on the barrier or from the functioning of the pyrotechnic charge, which are internal to the syringe.

The present invention will now be described in more
10 detail with the aid of Figure 1 which shows a partial cross-sectional view of a syringe according to the invention and which can be used to describe two shock wave generators.

15 Figure 1 shows a view of a syringe 10 before use, the downstream end of this syringe 10 still being closed by a hermetic stopper 15 which ensures asepsis of the inner part of the application guide 8.

20 According to this Figure 1, the application guide 8 is continued inside the trigger tube 1 and comprises, from downstream to upstream, a threaded ring 16 which ensures the immobilization of a fixed barrier 4 on a shoulder of the guide, this shoulder forming a central
25 opening in which the shock wave generator device 3 is placed, formed by a pellet of sensitive composite explosive, surmounted by a microdetonator which can be initiated by percussion. A weight 9 is able to slide in

the internal continuation of the application guide 8 and comprises a striker pin at its downstream end and a retainer groove in which there are engaged three balls 11 placed in radial perforations of this continuation.

- 5 These balls 11 bear on the inner surface of the trigger tube 1 and immobilize the hollow weight percussion 9 surmounted by a spring 13 compressed between this weight 9 and the bottom of the trigger tube 1, this tube 1 being held in the initial position by a lower
10 internal shoulder in contact with the application guide 8.

The powdered active principle fills a semi-ellipsoid cavity 7 situated on the downstream face 6 of the
15 barrier 4, and this principle is held by means of a thin film secured on the fixed barrier 4 and wedged by the threaded ring 16.

- In operation, after the stopper 15 has been removed and
20 the freed end of the application guide 8 has been applied in contact with the area of the epidermis chosen for injection of the active principle, the trigger tube 1 is pressed in order to compress the spring 13 until the inner groove 12 of this tube 1
25 arrives at the level of the three balls 11 which spread apart radially and release the hollow percussion weight 9 whose downstream point will strike the microdetonator, causing the explosive pellet in contact

with the upstream face 5 of the fixed barrier 4 to explode. The plane shock wave thus generated will reach the cavity 7 and simultaneously provoke the rupture of the thin film and the ejection of the active principle on the basis of a phenomenon of reversal and focusing similar to the phenomenon employed in hollow charges. The hollow weight 9, the spring 13 and the material 14 then have the function of absorbing the effects behind the detonation, and the shock absorbing system 2 of the application guide 8 attenuates the effect of compression in front, this sensation of annular compression largely masking the pricking sensation resulting from the penetration of the streamlined jet of active product into the epidermis and dermis.

According to an alternative embodiment which can be described with reference to this same figure, the plane shock wave is not produced by an explosive in contact with the barrier 4 in which the blind cavity 7 is formed. This alternative (not shown) requires the use of a solid weight which is continued downstream by a cylindrical striking peen which can engage in the bore obtained by removing the explosive and the detonator so as to strike the fixed barrier 4 directly. In this alternative, the spring 13 is not useful and the material 14 must be replaced by a pyrotechnic gas generator which can be activated by an external means, the trigger tube 1 being completely integral with the

application guide 8 and comprising an internal sheath deformable at the level of the three balls 11. In operation, the initiation of the pyrotechnic gas generator ensures a pressure increase in the chamber

5 between the trigger tube and the weight, until the pressure exerted on this weight causes the partial engagement of the three balls in the deformable sheath and frees this weight, of which the peen will strike the fixed barrier 4 and will generate a plane shock

10 wave with which it is possible to obtain the formation of a streamlined jet of the active product initially stored in globular form in the blind cavity 7.

Claims

1. A needleless syringe (10) for injecting active principle and comprising, from upstream to downstream, a propelling system consisting of a shock wave generator device, a barrier comprising an upstream face (5) and a downstream face (6), said downstream face (6) having at least one blind cavity (7) in which the active principle is accommodated, and an application guide (8) for applying said syringe (10) to the skin of the patient to be treated, characterized in that, on the one hand, the barrier (4) is fixed and resistant to the shock wave and, on the other hand, said barrier (4) ensures a good propagation of the shock wave.

2. The needleless syringe as claimed in claim 1, characterized in that the barrier (4) has a substantially plane and transverse upstream face (5).

3. The needleless syringe as claimed in either of claims 1 and 2, characterized in that the shock wave generator device (3) produces a plane shock wave on the upstream face (5) of the fixed barrier (4).

4. The needleless syringe as claimed in claim 1,
characterized in that each blind cavity (7) has an
opening transverse section which is at least equal
5 to each transverse section of this cavity (7).

10 5. The needleless syringe as claimed in either of
claims 1 and 4, characterized in that each cavity
(7) has a form of revolution about an axis
parallel to the direction of propagation of the
shock wave.

15 6. The needleless syringe as claimed in either of
claims 1 and 4, characterized in that a plurality
of cavities are distributed on the downstream face
(6) of said barrier (4).

20 7. The needleless syringe as claimed in one of claims
1 to 3, characterized in that the shock wave on
the upstream face (5) of the fixed barrier (4) is
produced by a weight which impacts said barrier
(4).

25 8. The needleless syringe as claimed in one of claims
1 to 3, characterized in that the device (3)
generating a shock wave on the upstream face (5)
of the fixed barrier (4) comprises a detonating

pyrotechnic charge.

9. The needleless syringe as claimed in one of the preceding claims, characterized in that the length of the application guide (8) is between 1 and 8 times the diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

10. The needleless syringe as claimed in claim 9, characterized in that the application guide (8) comprises a shock absorbing system (2).

Concerning point V

Reasoned statement according to Article 35(2) with regard to novelty, inventive activity and industrial applicability; citations and explanations supporting this statement

Reference is made to the following document:

D1: WO 96 25190 A (OXFORD BIOSCIENCES LTD;
BELLHOUSE BRIAN JOHN (GB); BELL JOHN (GB)) 22
August 1996 (22.8.1996)

1. The subject of independent claim 1 satisfies the requirements regarding novelty and inventive activity, Article 33(2) and (3) PCT.

Document D1, which is considered the closest prior art, describes a needleless syringe for injection of active principle, comprising, from upstream to downstream, a propelling system consisting of a shock wave generator device, a barrier comprising a downstream face having at least one blind cavity in which the active principle is accommodated, and an application guide for said syringe, from which the syringe forming the subject of claim 1 differs in that said barrier is fixed and resistant to the shock wave and said barrier ensures a good propagation of the shock wave.

The problem which the present invention sets out to solve can be considered as being that of forming more streamlined jets of solid active principle which have a high perforation capacity.

The problem is solved by said barrier which is fixed and resistant to the shock wave and is able to ensure a good transmission of the shock wave. The principle of focusing of the syringe is inspired by the "hollow charge" effect by which the shock wave produced on the upstream face of said fixed and resistant barrier propagates through the barrier and reaches the downstream face of the barrier. When the shock wave has reached the particles of active principle accommodated in the blind cavity situated in the downstream face of the barrier, these particles organize to form a convergent protuberance which changes into a streamlined jet when the shock wave has reached the downstream face of the barrier.

No document in the prior art discloses or renders evident the needleless syringe based on the "hollow charge" effect which includes a fixed and resistant barrier ensuring a good propagation of the shock wave in order to focus the jet of active principle.

2. Claims 2-10 are dependent on claim 1 and introduce additional characteristics of the needleless syringe defined by claim 1.

For this reason, claims 2-10 also satisfy the requirements under Article 33(2) and (3) PCT concerning novelty and inventive activity.

11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000
1001
1002
1003
1004
1005
1006
1007
1008
1009
1010
1011
1012
1013
1014
1015
1016
1017
1018
1019
1020
1021
1022
1023
1024
1025
1026
1027
1028
1029
1030
1031
1032
1033
1034
1035
1036
1037
1038
1039
1040
1041
1042
1043
1044
1045
1046
1047
1048
1049
1050
1051
1052
1053
1054
1055
1056
1057
1058
1059
1060
1061
1062
1063
1064
1065
1066
1067
1068
1069
1070
1071
1072
1073
1074
1075
1076
1077
1078
1079
1080
1081
1082
1083
1084
1085
1086
1087
1088
1089
1090
1091
1092
1093
1094
1095
1096
1097
1098
1099
1100
1101
1102
1103
1104
1105
1106
1107
1108
1109
1110
1111
1112
1113
1114
1115
1116
1117
1118
1119
1120
1121
1122
1123
1124
1125
1126
1127
1128
1129
1130
1131
1132
1133
1134
1135
1136
1137
1138
1139
1140
1141
1142
1143
1144
1145
1146
1147
1148
1149
1150
1151
1152
1153
1154
1155
1156
1157
1158
1159
1160
1161
1162
1163
1164
1165
1166
1167
1168
1169
1170
1171
1172
1173
1174
1175
1176
1177
1178
1179
1180
1181
1182
1183
1184
1185
1186
1187
1188
1189
1190
1191
1192
1193
1194
1195
1196
1197
1198
1199
1200
1201
1202
1203
1204
1205
1206
1207
1208
1209
1210
1211
1212
1213
1214
1215
1216
1217
1218
1219
1220
1221
1222
1223
1224
1225
1226
1227
1228
1229
1230
1231
1232
1233
1234
1235
1236
1237
1238
1239
1240
1241
1242
1243
1244
1245
1246
1247
1248
1249
1250
1251
1252
1253
1254
1255
1256
1257
1258
1259
1260
1261
1262
1263
1264
1265
1266
1267
1268
1269
1270
1271
1272
1273
1274
1275
1276
1277
1278
1279
1280
1281
1282
1283
1284
1285
1286
1287
1288
1289
1290
1291
1292
1293
1294
1295
1296
1297
1298
1299
1300
1301
1302
1303
1304
1305
1306
1307
1308
1309
1310
1311
1312
1313
1314
1315
1316
1317
1318
1319
1320
1321
1322
1323
1324
1325
1326
1327
1328
1329
1330
1331
1332
1333
1334
1335
1336
1337
1338
1339
1340
1341
1342
1343
1344
1345
1346
1347
1348
1349
1350
1351
1352
1353
1354
1355
1356
1357
1358
1359
1360
1361
1362
1363
1364
1365
1366
1367
1368
1369
1370
1371
1372
1373
1374
1375
1376
1377
1378
1379
1380
1381
1382
1383
1384
1385
1386
1387
1388
1389
1390
1391
1392
1393
1394
1395
1396
1397
1398
1399
1400
1401
1402
1403
1404
1405
1406
1407
1408
1409
1410
1411
1412
1413
1414
1415
1416
1417
1418
1419
1420
1421
1422
1423
1424
1425
1426
1427
1428
1429
1430
1431
1432
1433
1434
1435
1436
1437
1438
1439
1440
1441
1442
1443
1444
1445
1446
1447
1448
1449
1450
1451
1452
1453
1454
1455
1456
1457
1458
1459
1460
1461
1462
1463
1464
1465
1466
1467
1468
1469
1470
1471
1472
1473
1474
1475
1476
1477
1478
1479
1480
1481
1482
1483
1484
1485
1486
1487
1488
1489
1490
1491
1492
1493
1494
1495
1496
1497
1498
1499
1500
1501
1502
1503
1504
1505
1506
1507
1508
1509
1510
1511
1512
1513
1514
1515
1516
1517
1518
1519
1520
1521
1522
1523
1524
1525
1526
1527
1528
1529
1530
1531
1532
1533
1534
1535
1536
1537
1538
1539
1540
1541
1542
1543
1544
1545
1546
1547
1548
1549
1550
1551
1552
1553
1554
1555
1556
1557
1558
1559
1560
1561
1562
1563
1564
1565
1566
1567
1568
1569
1570
1571
1572
1573
1574
1575
1576
1577
1578
1579
1580
1581
1582
1583
1584
1585
1586
1587
1588
1589
1590
1591
1592
1593
1594
1595
1596
1597
1598
1599
1600
1601
1602
1603
1604
1605
1606
1607
1608
1609
1610
1611
1612
1613
1614
1615
1616
1617
1618
1619
1620
1621
1622
1623
1624
1625
1626
1627
1628
1629
1630
1631
1632
1633
1634
1635
1636
1637
1638
1639
1640
1641
1642
1643
1644
1645
1646
1647
1648
1649
1650
1651
1652
1653
1654
1655
1656
1657
1658
1659
1660
1661
1662
1663
1664
1665
1666
1667
1668
1669
1670
1671
1672
1673
1674
1675
1676
1677
1678
1679
1680
1681
1682
1683
1684
1685
1686
1687
1688
1689
1690
1691
1692
1693
1694
1695
1696
1697
1698
1699
1700
1701
1702
1703
1704
1705
1706
1707
1708
1709
1710
1711
1712
1713
1714
1715
1716
1717
1718
1719
1720
1721
1722
1723
1724
1725
1726
1727
1728
1729
1730
1731
1732
1733
1734
1735
1736
1737
1738
1739
1740
1741
1742
1743
1744
1745
1746
1747
1748
1749
1750
1751
1752
1753
1754
1755
1756
1757
1758
1759
1760
1761
1762
1763
1764
1765
1766
1767
1768
1769
1770
1771
1772
1773
1774
1775
1776
1777
1778
1779
1780
1781
1782
1783
1784
1785
1786
1787
1788
1789
1790
1791
1792
1793
1794
1795
1796
1797
1798
1799
1800
1801
1802
1803
1804
1805
1806
1807
1808
1809
1810
1811
1812
1813
1814
1815
1816
1817
1818
1819
1820
1821
1822
1823
1824
1825
1826
1827
1828
1829
1830
1831
1832
1833
1834
1835
1836
1837
1838
1839
1840
1841
1842
1843
1844
1845
1846
1847
1848
1849
1850
1851
1852
1853
1854
1855
1856
1857
1858
1859
1860
1861
1862
1863
1864
1865
1866
1867
1868
1869
1870
1871
1872
1873
1874
1875
1876
1877
1878
1879
1880
1881
1882
1883
1884
1885
1886
1887
1888
1889
1890
1891
1892
1893
1894
1895
1896
1897
1898
1899
1900
1901
1902
1903
1904
1905
1906
1907
1908
1909
1910
1911
1912
1913
1914
1915
1916
1917
1918
1919
1920
1921
1922
1923
1924
1925
1926
1927
1928
1929
1930
1931
1932
1933
1934
1935
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
1954
1955
1956
1957
1958
1959
1960
1961
1962
1963
1964
1965
1966
1967
1968
1969
1970
1971
1972
1973
1974
1975
1976
1977
1978
1979
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
2025
2026
2027
2028
2029
2030
2031
2032
2033
2034
2035
2036
2037
2038
2039
2040
2041
2042
2043
2044
2045
2046
2047
2048
2049
2050
2051
2052
2053
2054
2055
2056
2057
2058
2059
2060
2061
2062
2063
2064
2065
2066
2067
2068
2069
2070
2071
2072
2073
2074
2075
2076
2077
2078
2079
2080
2081
2082
2083
2084
2085
2086
2087
2088
2089
2090
2091
2092
2093
2094
2095
2096
2097
2098
2099
2100
2101
2102
2103
2104
2105
2106
2107
2108
2109
2110
2111
2112
2113
2114
2115
2116
2117
2118
2119
2120
2121
2122
2123
2124
2125
2126
2127
2128
2129
2130
2131
2132
2133
2134
2135
2136
2137
2138
2139
2140
2141
2142
2143
2144
2145
2146
2147
2148
2149
2150
2151
2152
2153
2154
2155
2156
2157
2158
2159
2160
2161
2162
2163
2164
2165
2166
2167
2168
2169
2170
2171
2172
2173
2174
2175
2176
2177
2178
2179
2180
2181
2182
2183
2184
2185
2186
2187
2188
2189
2190
2191
2192
2193
2194
2195
2196
2197
2198
2199
2200
2201
2202
2203
2204
2205
2206
2207
2208
2209
2210
2211
2212
2213
2214
2215
2216
2217
2218
2219
2220
2221
222

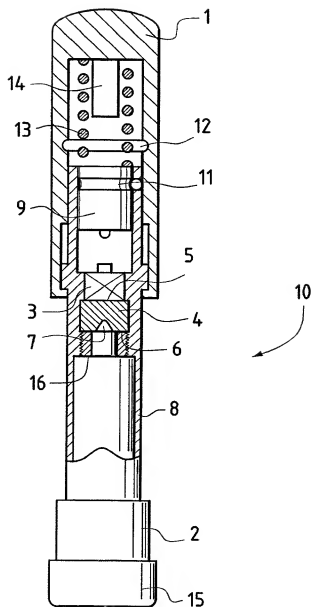


FIG.1

**DECLARATION AND POWER OF ATTORNEY
UNDER 35 USC §371(c)(4) FOR
PCT APPLICATION FOR UNITED STATES PATENT**

B 1117 PCT

As a below named inventor, I hereby declare that:
my residence, post office address and citizenship are as stated below under my name;

I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought, namely the invention entitled: Needleless syringe operating with a device generating a shock wave through a wall

described and claimed in international application number _____ filed _____.

I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations §1.56.

Under Title 35, U.S. Code §119, the priority benefits of the following foreign application(s) filed within one year prior to my international application are hereby claimed:

French Patent Application No 99 09255 filed on July 16, 1999

The following application(s) for patent or inventor's certificate on this invention were filed in countries foreign to the United States of America either (a) more than one year prior to my international application, or (b) before the filing date of the above-named foreign priority application(s):

I hereby appoint the following as my attorneys of record with full power of substitution and revocation to prosecute this application and to transact all business in the Patent Office:

(8)

James A. Oliff, Reg. No. 27,075; William P. Berridge, Reg. No. 30,024;

Kirk M. Hudson, Reg. No. 27,562; Thomas J. Pardini, Reg. No. 30,411;

Edward P. Walker, Reg. No. 31,450; Robert A. Miller, Reg. No. 32,771;

Mario A. Costantino, Reg. No. 33,565; and Caroline D. Dennison, Reg. No. 34,494.

ALL CORRESPONDENCE IN CONNECTION WITH THIS APPLICATION SHOULD BE SENT TO OLIFF & BERRIDGE, PLC, P.O. BOX 19928, ALEXANDRIA, VIRGINIA 22320, TELEPHONE (703) 836-6400.

I hereby declare that I have reviewed and understand the contents of this Declaration, and that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1	Typewritten Full Name of Sole or First Inventor	<u>Patrick</u> <u>ALEXANDRE</u>		
2	Inventor's Signature	Given Name	Middle Initial	Family Name
3	Date of Signature	<u>15 Dec. 2001</u>		
	Residence:	<u>GRAY</u>	Day	<u>FRANCE</u>
	Citizenship:	<u>FRANCE</u>	City	<u>FRX</u>
		State or Province		Country
	Post Office Address:	<u>14 avenue de la Libération - 70100 GRAY</u>		
	(Insert complete mailing address, including country)	<u>FRANCE</u>		

Note to Inventor: Please sign name on line 2 exactly as it appears in line 1 and insert the actual date of signing on line 3.

1
2
3

PAGE 2 OF U.S.A. DECLARATION FORM
(Discard this page in a sole inventor application)

B 1117 PC

1 **Typewritten Full Name**
of Second Joint Inventor (if any)

2-00

Pierre

BRUNET

Given Name

Middle Initial

Family Name

2 **Inventor's Signature:

PBRUNES

3 **Date of Signature:

January

16

2002

Month

Day

Year

Residence:

LARDY

City

State or Province

FRANCE

Country

Citizenship:

FRANCAISE

FRX

Post Office Address:
(Insert complete
mailing address,
including country)

17 rue Honville - 91510 LARDY

FRANCE

1 **Typewritten Full Name**
of Third Joint Inventor (if any)

3-00

Brigitte

CAGNON

Given Name

Middle Initial

Family Name

2 **Inventor's Signature:

Brigitte CAGNON

3 **Date of Signature:

January

16

2002

Month

Day

Year

Residence:

BALLANCOURT

City

State or Province

FRANCE

Country

Citizenship:

FRANCAISE

FRX

Post Office Address:
(Insert complete
mailing address,
including country)

24 Lotissement du Bois - 91610 BALLANCOURT

FRANCE

1 **Typewritten Full Name**
of Fourth Joint Inventor (if any)

4-00

claude

MIKLER

Given Name

Middle Initial

Family Name

2 **Inventor's Signature:

December

19

2001

Month

Day

Year

Residence:

DIJON

City

State or Province

FRANCE

Country

Citizenship:

FRANCAISE

FRX

Post Office Address:
(Insert complete
mailing address,
including country)

117 avenue du Drapeau - 21000 DIJON

FRANCE

1 **Typewritten Full Name**
of Fifth Joint Inventor (if any)

Given Name

Middle Initial

Family Name

2 **Inventor's Signature:

3 **Date of Signature:

Month

Day

Year

Residence:

City

State or Province

Country

Citizenship:

Post Office Address:

(Insert complete
mailing address,
including country)

**Note to Inventors: Please sign name exactly as it appears and insert the actual date of signing.

This form may be executed only when attached to the first page of the Declaration and Power of Attorney form of the application to which it pertains.